Clinical trial results:
Phase II, Open Label, Single Arm Study Assessing the Clinical Benefit of SAR125844, Administered as Single Agent by Weekly Intravenous (IV) Infusion, for the Treatment of Patients With Advanced Pretreated Non-Small Cell Lung Cancer (NSCLC) Harboring MET Gene Amplification

Summary

EudraCT number	2014-005696-93
Trial protocol	BE HU DE ES NL CZ GR FR AT PL IT
Global end of trial date	05 January 2016

Results information

Result version number	v1 (current)
This version publication date	05 January 2017
First version publication date	05 January 2017

Trial information

Trial identification

Sponsor protocol code	ACT14205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02435121
WHO universal trial number (UTN)	U1111-1163-1136

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 February 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 January 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the objective response rate (ORR), according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 reviewed by an Independent Third Party Review, of SAR125844 in subjects with advanced pretreated NSCLC harboring MET gene amplification.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 1 site in Belgium from 09 November 2015 to 05 January 2016.

Pre-assignment

Screening details:

Out of 153 subjects pre-screened, only 1 subject was enrolled and treated in the study. This subject discontinued due to disease progression (DP) and considered as completed (as per protocol).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	SAR125844

Arm description:

SAR125844 570 mg/m^2 intravenous (IV) infusion over 3 hours once weekly in each cycle (each cycle of 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.

Arm type	Experimental
Investigational medicinal product name	SAR125844
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SAR125844 570 mg/m^2 once weekly.

Number of subjects in period 1	SAR125844
Started	1
Treated	1
Completed	1

Baseline characteristics

Reporting groups	
Reporting group title	SAR125844
Reporting group description:	
SAR125844 570 mg/m^2 intravenous (IV) infusion over 3 hours once weekly in each cycle (each cycle of 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.	

Reporting group values	SAR125844	Total	
Number of subjects	1	1	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	0	0	

End points

End points reporting groups

Reporting group title	SAR125844

Reporting group description:

SAR125844 570 mg/m^2 intravenous (IV) infusion over 3 hours once weekly in each cycle (each cycle of 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.

Primary: Percentage of Subjects With Objective Response

End point title	Percentage of Subjects With Objective Response[1]

End point description:

Objective response rate was defined as the percentage of subjects from the assessed population with complete response (CR) or partial response (PR) according to the RECIST version 1.1. CR was defined as disappearance of all target and non-target lesions and normalization of tumor marker level. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. An objective response was confirmed at least 4 weeks after the first documentation of response.

End point type	Primary

End point timeframe:

Baseline up to DP, death or study cut-off, whichever came first (maximum duration: 58 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[2] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

DOR was defined as the time (in weeks) from the first documentation of objective tumor response (CR or PR) that was subsequently confirmed, to the first documentation of DP or death (due to any cause), whichever occurred first. In the absence of DP or death, the DOR should be censored at the date of the last tumor assessment or the cutoff date, whichever occurs first.

End point type	Secondary

End point timeframe:

From the time of the first documented evidence of a confirmed CR or PR until DP, death or study cut-off, whichever came first (maximum duration: 58 days)

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: weeks				
median (confidence interval 95%)	(to)			

Notes:

[3] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

PFS was defined as time interval (in months) between the date of the first infusion of SAR125844 to the date of first documentation of tumor progression or death due to any cause, whichever occurs first. In the absence of DP or death, the subject was to be censored at the date of the last tumor assessment or the cut-off date, whichever occurs first. DP was defined using RECIST version 1.1 as: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study or unequivocal progression of existing non-target lesion. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered progression.

End point type	Secondary

End point timeframe:

Baseline up to DP, death or study cut-off, whichever came first (maximum duration: 58 days)

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[4] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

OS was defined as the time interval (in months) from the date of first infusion of SAR125844 to the date of death due to any cause. In the absence of death, the subject was to be censored at the last date the subject was known to be alive or the analysis cut-off date if the subject was known to be alive after analysis cut-off date.

End point type	Secondary

End point timeframe:

Baseline up to death or study cut-off date, whichever came first (maximum duration: 58 days)

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[5] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) for SAR125844

End point title	Maximum Observed Plasma Concentration (Cmax) for SAR125844

End point description:

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before the end of infusion (EOI), 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: mcg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[6] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve (AUC) for SAR125844

End point title	Area Under the Concentration-Time Curve (AUC) for SAR125844

End point description:

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: mcg*h/mL				
arithmetic mean (standard deviation)	()			

Notes:

[7] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) for SAR125844

End point title	Clearance (CL) for SAR125844

End point description:

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Litre/hour				
arithmetic mean (standard deviation)	()			

Notes:

[8] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss) for SAR125844

End point title	Volume of Distribution at Steady State (Vss) for SAR125844

End point description:

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: Litre				
arithmetic mean (standard deviation)	()			

Notes:

[9] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) for SAR125844

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) for SAR125844

End point description:

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1: 5 minutes before EOI, 15 minutes, 1 hour, 2.5 to 3 hours, 4 hours and 45 hours after EOI

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: Hours				
median (full range (min-max))	(to)			

Notes:

[10] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (EORTC QLQ-C30) at Day 1 of Each Cycle and at End of Treatment (EOT)

End point title	Change From Baseline in European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (EORTC QLQ-C30) at Day 1 of Each Cycle and at End of Treatment (EOT)

End point description:

The EORTC QLQ-C30 is a 30-item questionnaire to assess the overall quality of life in cancer subjects. It includes five functional scales (physical, role, cognitive, emotional, and social), global health status/quality of life, disease/treatment related symptoms scales (fatigue, pain, nausea/vomiting) and

other single items (dyspnea, appetite loss, constipation, insomnia, diarrhoea and financial difficulties). 28 questions used 4 point scale (1 "Not at all" to 4 "Very much"); 2 questions used 7-point scale (1 "Very poor" to 7 "Excellent"). Scores were averaged and transformed to 0-100 scale; higher scores indicated better level of functioning or greater degree of symptoms.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), then Day 1 of each cycle (before SAR125844 administration) and at EOT (30 days after last dose) (maximum duration: 58 days)

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[11]			
Units: units on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[11] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EORTC Quality of Life Questionnaire-Lung Cancer 13 (QLQ-LC13) Score at Day 1 of Each Cycle and at EOT

End point title	Change From Baseline in EORTC Quality of Life Questionnaire-Lung Cancer 13 (QLQ-LC13) Score at Day 1 of Each Cycle and at EOT

End point description:

QLQ-LC13 consisted of 13 questions relating to disease symptoms specific to lung cancer and treatment side effects typical of treatment with chemotherapy and radiotherapy experienced during past 1 week. The 13 questions comprised 1 multi-item scale for dyspnea and 10 single-item symptoms and side effects (coughing, hemoptysis, sore mouth, dysphagia, peripheral neuropathy, alopecia, chest pain, arm pain, other pain, and medicine for pain). Response ranges from 1 "not at all" to 4 "very much". Scores for each item were transformed to 0 to 100 , where higher symptom score = greater degree of symptoms.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), then Day 1 of each cycle (before SAR125844 administration) and at EOT (30 days after last dose) (maximum duration: 58 days)

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: units on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[12] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cancer Therapy Satisfaction Questionnaire (CTSQ) Score at Day 1 of Cycle 4 and at EOT

End point title	Change From Baseline in Cancer Therapy Satisfaction Questionnaire (CTSQ) Score at Day 1 of Cycle 4 and at EOT

End point description:

CTSQ is a validated 16-item questionnaire that measures three domains related to subject's satisfaction with cancer therapy. These include expectations of therapy (5 questions), feelings about side effects (4 questions), and satisfaction with therapy (7 questions). All questions were assessed on a 5-point scale; 1=never to 5=always. Scores from all questions were averaged and transformed to provide a total score range of 0-100; where higher scores represent better health.

End point type	Secondary

End point timeframe:

Baseline (Day 1 of Cycle 1), then Day 1 of Cycle 4 (before SAR125844 administration) and at EOT (30 days after last dose) (maximum duration: 58 days)

End point values	SAR125844			
Subject group type	Reporting group			
Number of subjects analysed	0[13]			
Units: units on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[13] - Endpoint was not analyzed as study terminated prematurely due to unsatisfactory subject recruitment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (58 days) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are treatment emergent that is AEs that developed/worsened that occurred during 'the treatment emergent period' (time from first dose of study drug until 30 days after the last administration of study drug).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	SAR125844

Reporting group description:

SAR125844 570 mg/m^2 IV infusion over 3 hours once weekly in each cycle (each cycle of 3 weeks) until unacceptable toxicity, DP, or consent withdrawal.

Serious adverse events	SAR125844		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	SAR125844		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	 1 / 1 (100.00%) 1 1 / 1 (100.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 November 2015	The study was terminated prematurely due to unsatisfactory subject recruitment.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None of the endpoints were analysed as the study was terminated prematurely due to unsatisfactory subject recruitment.

Notes: